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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/970,043	10/02/2001	Jae Hyong Byon	KBPCO.001APC	8684

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EXAMINER
MCINTOSH III, TRAVISS C

ART UNIT	PAPER NUMBER
1621	6

DATE MAILED: 08/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

To Be Filed

Office Action Summary	Application N .	Applicant(s)	
	09/970,043	BYON ET AL.	
	Examiner	Art Unit	
	Traviss C McIntosh	1621	

-- Th MAILING DATE of this communication appears on the cover sh t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Korea on February 3, 2000. It is noted, however, that applicant has not filed a certified copy of the 2000/5294 application as required by 35 U.S.C. 119(b).

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Korea on December 28, 2000. It is noted, however, that applicant has not filed a certified copy of the 2000/83853 application as required by 35 U.S.C. 119(b).

Acknowledgment is made of applicant's claim for foreign priority based on PCT/KR01/00139 filed on February 1, 2001. It is noted, however, that applicant has not filed a certified copy of the application as required by 35 U.S.C. 119(b).

Information Disclosure Statement

The information disclosure statement filed on February 5, 2002 is being taken into consideration only in light of the portion which was translated into English. However, the references titled "Effect of pH Drug Release From Polysaccharide Stirred Cell", and "A Cardiovascular Support System Containing Potent Antioxidants" in the information disclosure statement filed fail to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because they have been supplied in illegible and incomplete copies. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of

filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 56-60 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Experimentation is a conclusion reached by weighing the noted factual considerations set forth below as seen in ***In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)***. A conclusion of lack of enablement means that, based on the evidence regarding a fair evaluation of an appropriate combination of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

These factors include:
(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims - The nature of the invention

Claims 56-60 are drawn to preventing hyperlipidemia, obesity, and diabetes in patients by administering a pharmaceutical composition comprising a polymannuronate and a carrier.

The state of the prior art

Polymannuronate compositions are known in the art to be useful in lowering cholesterol levels and treating diabetes and obesity, as seen in Eliaz et al 6,274,566. The art does not teach that the polymannuronate compositions will prevent these conditions.

The level of predictability in the art

The examiner acknowledges the probability and predictability that the active agent, which is polymannuronate, indeed has efficacy in treating obesity and diabetes, however, the art appears to be silent with regard to the predictability of the prevention of obesity and diabetes in patients. In fact, the art does not teach the prevention of diabetes or obesity with any active agents or compounds. There is not seen sufficient data to substantiate the assertion that diabetes and obesity may be prevented by the use of polymannuronate compositions. One skilled in the art would not predict from the disclosure that obesity and diabetes can be prevented in view of the examples and data provided.

The amount of direction provided by the inventor

The instant specification is not seen to provide adequate guidance which would allow the skilled artisan to extrapolate from the disclosure and examples provided to enable the use of the low molecular weight polymannuronate composition to prevent obesity, diabetes and hyperlipidemia. Although the instant specification provides guidance for the treatment of the diseases, it is not seen to provide for the prevention of the diseases.

The existence of working examples

The working examples set forth in the instant specification are limited to the following combinations:

Example 1: drawn to a method of preparing polymannuronate

Example 2: drawn to hydrolysis of alginate with various organic acids

Example 3: drawn to the effects of polymannuronate diets on male Sprague Dawley rats

The examiner notes that none of these examples is seen to be sufficient to substantiate the preventive efficacy of polymannuronate for preventing obesity and diabetes in patients. The art does not teach or correlate the instant examples with prevention of obesity and diabetes in patients.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure

Indeed, in view of the information set forth supra, the instant disclosure is not seen to be sufficient to enable the prevention of diabetes, obesity and hyperlipidemia by administering a polymannuronate composition. As set forth in the claims, the skilled artisan would not extrapolate preventive efficacy from the results of the treatment modalities set forth in the Examples of the instant specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3, 7-9, 25, 27-29, 33-36, 41, 48-51, 53-59, and 61 are vague and indefinite as they all recite a molecular weight as a limitation and do not recite a unit of measure as to what the numerical value represents. Additionally, claims 30-32 and 38-40 recite limitations of viscosity where no units of measure are given as to determine what is meant to be encompassed by the instant application. The examiner respectfully requests the units of measure to be added to the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-11, 13-29, 33-37, and 51-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eliaz et al. (US Patent 6,274,566) in view of Dorian et al. (US Patent 5,639,467).

The claims of the instant invention are drawn to a method of preparing a polymannuronate composition comprising hydrolyzing alginate for about 20 minutes to 3 hours (preferably 1 – 1.5 hours) with an organic acid (acetic acid) having a concentration of about 0.2 – 0.6 M and heating, wherein the resulting mixture comprises polymannuronate and polyguluronate and the polymannuronate has a molecular weight in the range of 4,000 to 500,000 Daltons (preferably 40,000 – 50,000 Da). The polymannuronate is then isolated by adjusting the pH to a range from about 2.5 – 3.5 (preferably 2.8 – 3.0) by adding an organic acid thereby forming a precipitate in the mixture, then collecting the supernatant and precipitating the polymannuronate out of the supernatant giving a polymannuronate of about 70% - 98% pure (preferably 90 – 95% pure). The instant is additionally drawn to a polymannuronate composition having a molecular weight of about 40,000 – 50,000 Da. The instant application is additionally drawn to an isolated polymannuronate having a molecular weight of about 4,000 – 500,000 Da (40,000 to 50,000 preferably) and being about 80 – 97% pure. The instant application is also drawn to a pharmaceutical composition comprising polymannuronate having a molecular weight of about 4,000 – 500,000 Da (preferably 40,000 – 50,000 Da) and a carrier wherein if the composition comprises polyguluronate, the polyguluronate is less than 30% of the weight. Further, the instant application is drawn to a method of treating a patient in need of treatment for controlling cholesterol levels, lipid levels, and expelling heavy metals from a body by administering to the patient a pharmaceutical composition as noted above.

Eliaz et al. teach of low molecular weight alginates wherein high molecular weight algin can be reduced to low molecular weight products of 40,000 Daltons by acid hydrolysis (column 1, lines 54-57). The low molecular weight alginates which are derived from seaweeds (column 1, lines 47-48) as taught by Eliaz et al. are associated with the reduction of cholesterol, the treatment of diabetes, and for the treatment and/or removal of heavy metals from a patient (column 2, lines 5-23). Eliaz et al. additionally teach to combine the alginate with any pharmaceutical acceptable carrier suitable for administration (column 2, lines 60 – 67). What Eliaz et al. does not teach is the process of acid hydrolysis and isolation

Dorian et al. disclose a method of hydrolyzing alginate to polymannuronate. The molecular weight of the starting alginate is preferably 2,000 to 300,000 Daltons. The high molecular weight can be adjusted by acid hydrolysis wherein the initial alginate is dissolved in an acid solution having a concentration of about 0.1 – 0.5 M and heating until the desired molecular weight is obtained. The degree of hydrolysis is controlled by monitoring the molecular weight of the alginate and neutralizing the solution to stop the reaction, wherein a higher acid concentration results in faster hydrolysis (column 6, lines 49-67). Dorian et al additionally teach that the mannuronate to guluronate ratio can be increased or decreased by selective precipitation or by solubilization by organic solvents or acids (column 6, lines 43-46). Dorian et al. teach that by extracting alginate with an acidic solution, it is possible to selectively solubilize, thereby isolating the homopolymeric-rich alginates (polymannuronate being M-rich and polyguluronate being G-rich) where M-rich alginates are preferentially solubilized relative to G-rich alginates. Treatment of the solution with an acid precipitates the G-rich leaving the M-rich alginate in the solution. Separation of the precipitate (by centrifugation) from the solution gives fractions of

both G-rich and M-rich alginates respectively. After separation of the precipitate from the solution, the M-rich portion is precipitated out of the solution by addition of an acid or ethanol. The proportion of the material precipitated can be controlled and adjusted by adjusting the pH and preferably the resulting alginate is in the range of 10 – 95% (column 7, lines 1 – 36). What Dorian et al. does not teach is to hydrolyze the alginate for a time of 1 to 1.5 hours to obtain a product having a molecular weight in the range of 40,000 to 50,000 Da or to use the resulting product in compositions to treat diabetes, obesity, control cholesterol levels, expel heavy metals etc.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to hydrolyze the alginate by the process of Dorian et al. for a time as to obtain a polymannuronate having a molecular weight of 40,000 – 50,000 Da. and use it for the treatments as taught by Eliaz et al. One would be motivated to use the process as taught by Dorian et el to produce the low molecular weight polymannuronate and use the product in treatments as taught by Eliaz et al. as it is known in the art that the molecular weight of a natural algin can be decreased by acid hydrolysis and that algin has many desirable effects on human health. Further, algin is a natural substance derived from seaweed, and one would be motivated to use natural substances in pharmaceutical compositions as they are more acceptable by the human population.

Claims 41 – 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eliaz et al. and Dorian et al. as applied to the claim above, and further in view of Iwata et al (US Patent 5,324,526).

The claims of the instant application are drawn to the methods and compositions as noted above, and additionally to a nutritional composition comprising a foodstuff (beverage, ham, noodle, or margarine) and polymannuronate having a molecular weight of 4,000 – 500,000 Da (preferably 40,000 – 50,000 Da) where the polymannuronate is in the composition in an amount between 0.0001 – 15% based on the weight.

Iwata et al. teach of an algin-containing food which comprises an algin having an average molecular weight in the range of 10,000 – 900,000 Daltons. Additionally, Iwata et al. teach of an algin-containing beverage for the use as a health food comprising from 1 to 50% by weight of an algin having a average molecular weight in the range of 10,000 – 900,000 Daltons. Iwata et al. further teach that the resulting low molecular weight algin is effective for the prevention of obesity and diabetes (column 2, lines 52-68). For the ease of drinking, the algin as taught by Iwata et al. preferably has an average molecular weight of 10,000 to 150,000 Daltons and the algin may be any alginic acid or salt or an alginate ester (column 3, lines 32-40).

What is not taught by Iwata et al. is the process of hydrolyzing alginate or to specifically use polymannuronate as the alginate ester in the nutritional composition.

It would be obvious to one of ordinary skill in the art at the time the invention was made to incorporate the polymannuronate as taught by Eliaz et al. in the nutritional food composition as taught by Iwata et al. and to use the process of Dorian et al. to produce the specific low molecular weight alginate. One would be motivated to do so as humans prefer to ingest natural substances incorporated in their food as a means of obtaining health benefits rather than a substance which is not naturally derived.

Conclusion

Claims 1-61 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Traviss C McIntosh whose telephone number is 703-308-9479. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 703-308-4532. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

James O. Wilson
Group 1600
Primary Examiner

Traviss C. McIntosh
August 8, 2002